

COMPOUNDS FOR THE TREATMENT OF METABOLIC DISORDERS

5 CROSS-REFERENCE TO PRIOR APPLICATIONS

This is a divisional of U.S. Patent Application No. 10/167,839, filed June 12, 2002, the content of which is incorporated herein by reference. This application claims the benefit of U.S. Provisional Patent Application No. 60/297,282, filed June 12, 2001, the content of  
10 which is incorporated herein by reference.

BACKGROUND OF THE INVENTION

Diabetes mellitus is a major cause of morbidity and mortality. Chronically elevated blood  
15 glucose leads to debilitating complications: nephropathy, often necessitating dialysis or renal transplant; peripheral neuropathy; retinopathy leading to blindness; ulceration of the legs and feet, leading to amputation; fatty liver disease, sometimes progressing to cirrhosis; and vulnerability to coronary artery disease and myocardial infarction.

20 There are two primary types of diabetes. Type I, or insulin-dependent diabetes mellitus (IDDM) is due to autoimmune destruction of insulin-producing beta cells in the pancreatic islets. The onset of this disease is usually in childhood or adolescence. Treatment consists primarily of multiple daily injections of insulin, combined with frequent testing of blood glucose levels to guide adjustment of insulin doses, because excess insulin can cause  
25 hypoglycemia and consequent impairment of brain and other functions.

Type II, or noninsulin-dependent diabetes mellitus (NIDDM) typically develops in adulthood. NIDDM is associated with resistance of glucose-utilizing tissues like adipose tissue, muscle, and liver, to the actions of insulin. Initially, the pancreatic islet beta cells compensate by secreting excess insulin. Eventual islet failure results in decompensation  
30 and chronic hyperglycemia. Conversely, moderate islet insufficiency can precede or coincide with peripheral insulin resistance. There are several classes of drugs that are

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## COMPOUNDS FOR THE TREATMENT OF METABOLIC DISORDERS

### ABSTRACT

Compounds useful for the treatment of various metabolic disorders, such as insulin resistance syndrome, diabetes, hyperlipidemia, fatty liver disease, cachexia, obesity, atherosclerosis and arteriosclerosis, are disclosed.